Chapter XVIII

FUTURE COMMITMENTS

The large volume and complexity of the data collected during this baseline phase of the Ranch Hand II study have made it difficult to completely fulfill all aspects of the analytic plan envisioned in the study protocol. While most of the major anticipated analyses have been completed and included in this report, other important tasks remain to be done. The results cited in this report logically lead toward a commitment by the USAF and the study principal investigators to pursue further evaluations of these data, and follow the study participants over time. There are 5 key areas requiring additional effort: (1) database refinement, (2) definition of requirements and examination refinements for the follow-up phase of the study, (3) refinement and expansion of exposure indices (4) additional statistical analyses and (5) collaborative activities with other organizations involved in herbicide/dioxin research.

1. Database Refinement

The database derived from the questionnaire and from the physical examination was very extensive in size and scope, and a quality control program was initiated to identify coding, keypunching, and editing errors in the database provided by the contractors. This data validation has been an on-going task, and is not yet complete in some areas. After the remaining questionnaire and physical examination data have been validated by comparison with the source documents, epidemiologic and statistical analyses of these data will be completed. Additionally, validation of illnesses and conditions reported on the in-home questionnaire will continue to be accomplished as medical records and birth certificates are received. Methods of validating smoking histories, and a reassessment of flying status and its impact on compliance will be pursued. The completion of this process will provide a verified database for subsequent analyses. This process will also allow an assessment of the degree of differential reporting present in the study.

2. Follow-up Examination Requirements

One of the purposes of the baseline phase was to identify clinical areas requiring in-depth evaluation in the follow-up portions of the study. Focused questionnaire and physical examination formats will be developed for use during the reexamination scheduled for 1985. At that time detailed evaluation of skin cancer, and known risk factors affecting its occurrence will be obtained. Additional data on fertility and reproductive history will be gathered and updates of conceptions and live births occurring since the baseline questionnaire will be obtained. The cardiovascular status of the participants will also be closely examined, using doppler measurements of peripheral pulses and electrocardiographic monitoring during stress testing. New, fully validated psychological scales will be used to assess additional psychological parameters such as sleep patterns. Further immunologic evaluations with strict laboratory quality control will also be accomplished. Steps will also be taken to insure that all participants comply with dietary and 24-hour urine collection requirements. At

the time of the follow-up physical examination, all participants will be requested to authorize an autopsy at the time of their deaths and have copies of those reports and tissue specimens provided to the Air Force. The participants will also be asked to forward copies of hospitalization summaries and other significant medical events to the Air Force for inclusion in their records at Brooks AFB.

3. Exposure Index Refinement

The index of exposure to phenoxy herbicide and dioxin used in this report is not as complete or refined as planned in the study protocol. As it is currently calculated, each of the major occupational categories (Officers, Enlisted Flying, and Enlisted Ground) must be analyzed separately since the index is not necessarily equivalent in each category. A series of flights in a C-123 aircraft is planned. The aircraft will be configured and flown to simulate the Vietnam spray missions and a herbicide simulant will be released. Industrial hygiene sampling techniques will be used to measure differential exposure for aircrewmembers, ground support personnel, and administrative staff members. These data will then be used to calculate a weighting factor for use in the exposure index. In this way, a common index can be applied to all 3 occupational categories. The individual records of flying time ("Form 5's") will be used wherever possible to more clearly define the opportunity for in-flight exposures. Adjustment of the exposure analyses for confounding factors such as age and time spent in Southeast Asia will also be conducted to refine the index and make it more specifically a measure of herbicide exposure. This exposure index will also be modified to assess the degree of exposure to other chemicals such as arsenical herbicides (Herbicide Blue) and malathion.

4. Additional Statistical Analyses

Expanded statistical analyses and procedures are planned on the baseline data of this study. More detailed statistical power estimates will be developed for the analyses contained in this report, and an overall assessment of the ability of this study to detect adverse health effects in the populations studied will be made. Specifically, the analyses of reported and verified birth defects will be reaccomplished with the nature of the anomalies categorized as severe, moderate, and of minor medical consequence. The defects will also be classified as being congenital or teratogenic in origin. The results of the semen analyses and the father's occupation will also be considered. Efforts will be made to more fully define and correct sources of potential bias in the subsets of the comparison group so that all analyses can be conducted using the entire group of comparison individuals. This will maximize study power, and allow the use of the replacement strategy outlined in the protocol. Additional matched pair analyses will also be conducted in each clinical area, thus taking full advantage of the most powerful statistical techniques. The full spectrum of clinical end points and covariables will be analyzed as well. Case by case reviews of individuals with testicular, bladder, oropharyngeal, and skin cancer and those with pulse abnormalities will be conducted. This review may highlight additional risk factors and may suggest alternative epidemiologic and statistical methodologies for subsequent reanalysis (e.g., case-control studies).

Other techniques will be used to address correlations between clinical areas in the data. An organ system does not operate independently, and interactions between systems will be evaluated in subsequent reports. The effects of differential reporting are potentially significant in this study, and analyses aimed at differences in reporting between groups, and between study participants and their spouses will be evaluated. Questionnaire data was collected from the next-of-kin of deceased individuals and from totally noncompliant individuals, and time constraints have not permitted an analysis of these data. However, these are potentially valuable sources of information and appropriate evaluation will be conducted as time permits. Additional testing using more multi-variate techniques, expanded model-fitting, and goodness-of-fit testing will also be carried out via contract.

5. Collaborative Activities

Over the past 5 years, the principal investigators have worked closely with other organization and scientists involved in the herbicide/dioxin issue, and these collaborative activities will be strengthened and expanded. The common problems encountered by this study and the studies of Vietnam veterans being conducted by the Centers for Disease Control and the Veterans Administration can be more effectively resolved through the sharing of approaches and solutions. Collaboration has benefited all of these studies in the past, and should continue to be of benefit in the future. In addition to U.S. governmental agencies, the principal investigators have interacted with the epidemiologic staffs at DOW Chemical Company, Monsanto Company and with researchers in Australia, New Zealand and Europe. The value of these interactions cannot be overstated, and these contacts will be maintained as the study progresses. More importantly, a closer working relationship will be developed between the principal investigators and the Advisory Committee on Special Studies Relating to the Possible Long-Term Health Effects of Phenoxy Herbicide and Contaminants. Continued coordination with this panel will be invaluable as the complex findings of this study emerge over time.